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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/730,323	BOLLA ET AL.	
	Examiner	Art Unit	
	NANCY VOGEL	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2007 and 26 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *29-39 and 43-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-39 and 43-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 29-39, 43-50 are pending in the case.

Any rejection of record in the previous action not addressed in this office action is withdrawn.

Claim Rejections - 35 USC § 112

Claims 29-39, 43-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained essentially for the reasons made of record in the previous Office action, mailed 5/16/07.

Applicant's arguments filed 8/16/07 have been considered but have not been found convincing.

Applicants have argued that "[A]s amended, the ration of amino acids in the polypeptide encoded by the construct of Claim 37-39 or expressed by the transformed yeast strains of claim 29-36 are governed by the dietary need of the animal and the particular feed source selected. The specification at page 7-8, and again in Example 9 at page 29-31 provide ample showing of how the dietary requirements may be determined". However, it is maintained that the claims still recite that the yeast used as a feed supplement should comprise a nucleic encoding the appropriate types and

rations of amino acids, such that the desired result, ie. weight gain when compared to the weight gained with any particular feed source, for any particular animal, as has been previously argued. The sections of the specification pointed to by applicant for support, disclose general guidance of "how the dietary requirements may be determined", however, there is no specific disclosure of adequate representative information which provides enough description showing that the invention as claimed was in possession of the inventor at the time of filing. The examples in the specification are only representative of one such transformed yeast strain and the results are not predictive of any other yeast strains/ nucleic acid constructs capable of being produced by a yeast such that the ratio of amino acids, when added to a predetermined feed source causes weight gain in increased amount when compared to the feed source alone. Therefore, the rejection is maintained.

Claims 44-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

The specification as originally filed does not provide support for the invention as now claimed: “wherein methionine/cysteine may be either methionine or cysteine” (claims 39, 44-50); “a ratio of about 100:60:60:75:60:80:20"(claim 44); “a ratio of about 100:100::33:15:67:100:75:100:75:67:33:67” (claim 47) and “a ratio of about

100:100:33:15:67:100:75:100:75:75:20:50" (claim 48); "a ration of about 100:15:100:85:50:20:20" (claim 49); "a ratio of about 100:10:50:10:25" (claim 50). The Table 2, Table 5, and Table 6 and Example 9 pointed to by applicant for support does not disclose these particular numbers, or the terms "about" in reference to the figures disclosed. There appears to be no support in the specification for the definition of "methionine/cysteine" as now recited in the claim. This a new matter rejection. The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned limitations, as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 45 is vague and indefinite in the recitation of "a polypeptide comprising the following amino acid units: lysine, and methionine/cysteine, and histidine, in a ration of

about 3 : 1", since only two terms are present in the ratio, although three amino acids are recited. Therefore, it is unclear what the ratio of amino acids is intended to be.

Claim Rejections - 35 USC § 102

Claims 29, 30, 32-34, 36, 27, 43 rejected under 35 U.S.C. 102(b) as being anticipated by Barr et al.

It is noted that applicants have amended the claims to recite that the amino acids in the peptide expressed in the claimed yeast strain are those such that the weight increase the target animal gains when fed on a predetermined feed source is less than when the feed supplement (i.e. the transformed yeast) is fed in addition to the feed source. However, it is considered that any yeast strain expressing virtually any peptide of at least two amino acids would cause weight gain when added to a feed source, since it would be a source of amino acids. Therefore, applicant's amendments do not substantially change the subject matter of the claims.

This rejection is maintained essentially for reasons made of record in the previous Office action.

Applicants arguments filed 8/16/07 have been considered but have not been found convincing.

Applicants have argued that "Barr merely teaches a yeast strain transformed with a construct containing a gene encoding an exogenous protein" and "Barr does not teach or suggest that the composition of the exogenous protein is determined by the nutritional requirement of the specific animal and the type of diet the animals are

normally fed". However, the claims are not drawn to a method of determining optimum ratios of amino acids for animal feed supplement; rather they are drawn to a transformed yeast comprising a protein having the ability to cause weight gain for an animal when added to a feed source. Therefore, it is maintained that the reference meets those limitations.

Claims 29-30, 32-34, 36-37, 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Nussenzweig et al. (US Patent 4,826,957) as evidence by Barr et al. (both previously cited) .

It is noted that applicants have amended the claims to recite that the amino acids in the peptide expressed in the claimed yeast strain are those such that the weight increase the target animal gains when fed on a predetermined feed source is less than when the feed supplement (i.e. the transformed yeast) is fed in addition to the feed source. However, it is considered that any yeast strain expressing virtually any peptide of at least two amino acids would cause weight gain when added to a feed source, since it would be a source of amino acids. Therefore, applicant's amendments do not substantially change the subject matter of the claims.

This rejection is maintained essentially for reasons made of record in the previous Office action.

Applicants arguments filed 8/16/07 have been considered but have not been found convincing.

Applicants have argued that "'957 merely teaches the exogenous of an exogenous protein in yeast, nothing was mentioned with regard to haw the composition

of the protein is designed based on the notional requirement of the specific animal and the type of diet the animals are normally fed". However, as is argued above, the claims are not drawn to a method of determining optimum ratios of amino acids for animal feed supplement; rather they are drawn to a transformed yeast comprising a protein having the ability to cause weight gain for an animal when added to a feed source. Therefore, the rejection is maintained.

Claims 29-32, 34, 36, 37, 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Tully et al. (US Patent 6,337,193) (previously cited).

It is noted that applicants have amended the claims to recite that the amino acids in the peptide expressed in the claimed yeast strain are those such that the weight increase the target animal gains when fed on a predetermined feed source is less than when the feed supplement (i.e. the transformed yeast) is fed in addition to the feed source. However, it is considered that any yeast strain expressing virtually any peptide of at least two amino acids would cause weight gain when added to a feed source, since it would be a source of amino acids. Therefore, applicant's amendments do not substantially change the subject matter of the claims.

This rejection is maintained essentially for reasons made of record in the previous Office action.

Applicants arguments filed 8/16/07 have been considered but have not been found convincing.

Applicants have argued that "Tully et al. does not disclose the claim limitation of determining the amino acid requirement of an animal fed with a particular diet and thus

the transformed yeast strain of Tully is distinguishable from the presently claimed yeast strain in the composition of the introduced construct". However, the claims are not drawn to a method of determining optimum ratios of amino acids for animal feed supplement; rather they are drawn to a transformed yeast comprising a protein having the ability to cause weight gain for an animal when added to a feed source. Therefore, the rejection is maintained.

Claims 29-37, 39, 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Cheng et al. (US Patent No. 5,985,605) (previously cited).

This rejection is maintained essentially for the reasons made of record, with addition of claims 35 and 39 to the rejection as necessitated by applicants amendments.

Cheng et al. teach a transformed yeast strain comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast (S. ruminantium JY35 phytase) under the control of a yeast derived promoter, said nucleic acid polymer selected from the group consisting of synthetic and natural nucleic acid polymers (see entire document, especially Fig 15, col. 5 lines 54-58, col. 3, lines 66-67 through col. 4, lines 1-15, col. 7, lines 44-65). Cheng et al. teach such a strain wherein the expression of the polypeptide is inducible (see col. 9 lines 11-36). Regarding claim 32, the polypeptide produced by the transformed yeast is retained in the yeast insofar as the transformed cells may or may not secrete the exogenous protein (see col. 7, lines 57-59). Regarding claim 34, the transformed yeast strain is P. pastoris of S. cerevisiae (see col. 7 lines 44-49). Regarding claims 35 and 39, the polypeptide comprises at

least 3 methionines, 6 histidines, 2 threonine, 2 isoleucines 1 valine, and 1 tryptophan; or 6 lysines, 3 methionines or cysteines, 2 threonines, 1 valine, 2 isoleucine, 6 histidine, and 1 tryptophan (see Fig. 15). Regarding claim 36 a promoter utilized is GAPDH promoter. Regarding claim 43, Cheng et al. also teach a method for producing this yeast additive comprising inserting such a construct into a yeast strain and expressing the gene (see col. 12, lines 56-67 and col. 13, lines 1-9).

Applicants have argued that for the reasons similar to those presented in the previous sections, applicant traverses this rejection because the '605 patent lacks teachings on determining the amino acid requirement of an animal fed with a particular grain in order to design the composition of the DNA construct to be introduced into the yeast strain. However, the claims are not drawn to a method of determining optimum ratios of amino acids for animal feed supplement; rather they are drawn to a transformed yeast comprising a protein having the ability to cause weight gain for an animal when added to a feed source. It is maintained that the protein disclosed in the reference fulfills this limitation. Therefore, the rejection is maintained.

Claims 29-37, 39 and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Lei et al. (US Patent 6,451,572) (previous cited) and Dassa et al. (J. Bacteriol., 172, 9, 5497-5500, 1990, cited for evidence only).

This rejection is maintained essentially for the reasons made of record, with addition of claims 35 and 39 to the rejection as necessitated by applicants amendments.

Lei teaches a transformed yeast strain comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to yeast (see, i.e. the appA gene of E. coli at col. 5, lines 63-64) under the control of a yeast derived promoter , said nucleic acid polymer selected from the group consisting of synthetic and natural nucleic acid polymers (see entire document, exp. Col. 5, lines 45-67, col. 6, lines 33-37, col. 8 lines 9-56). Regarding claim 30, Lei teaches such a strain wherein expression of the polypeptide strain is inducible (se col. 8 lines 11-36). Regarding claim 31, Lei teaches such a strain wherein the polymer may be inserted into the host strain's genome , (col. 7 lines 39-41). Regarding claim 32, the polypeptide produced is retained by the transformed yeast insofar as the transformed cells do not secrete the exogenous protein (see col. 7, lines 19-34). Regarding claim 33, the transformed yeast cell is auxotrophic, but was non-auxotrophic prior to transformation, as would be the case with the use of URA 3 as a selectable marker (see col. 8, lines 50-56). Regarding claim 34, the transformed yeast strain is S. cerevisiae (see col. 6 lines 3-37). Regarding claims 35 and 39, the appA gene of E. coli encodes a polypeptide that comprises (at least) least 3 methionines, 6 histidines, 2 threonine, 2 isoleucines 1 valine, and 1 tryptophan; or 6 lysines, 3 methionines or cysteines, 2 threonines, 1 valine, 2 isoleucine, 6 histidine, and 1 tryptophan (see Dassa et al., J. Bacteriol. 172, 9, 5497-5500, 1990, Fig. 2, cited for evidence only). Regarding claim 36, a promoter utilized for the production of phytase is the GAPDH promoter (see col. 8, lines 9-18). Regarding claim 37, Lei also teaches the construct for transforming a host organism (yeast) comprising a nucleic acid polymer for encoding a polypeptide ordinarily exogenous to said organism and a promoter, wherein

the nucleic acid polymer is a plasmid and is used to make a protein that would be capable of complementing a deficiency in a predetermined feed source, such as a deficiency in amino acids (i.e. protein) that would cause weight gain when added to said feed source (see e.g. col. 7, lines 36-37, and col. 8 lines 1-28). Regarding claim 43, Lei also teaches a method for producing this yeast additive comprising inserting such a construct into a yeast strain and expressing the gene (see Ex. 4, at col. 16 and Ex. 7 at col. 20).

Applicants argue that Lei does not mention how the composition of the protein is designed. Again, as has been argued above, the claims are not drawn to a method of determining optimum ratios of amino acids for animal feed supplement; rather they are drawn to a transformed yeast comprising a protein having the ability to cause weight gain for an animal when added to a feed source. Therefore, the rejection is maintained.

Claim Rejections - 35 USC § 103

Claims 29-39, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lei et al. ('572 patent cited above) as evidenced by Dassa et al. (cited above) in view of Sikorski et al. (Genetics 122:19-27, 1989).

This rejection is maintained essentially for the reasons made of record in the previous Office action, with claims 35 and 39 added as necessitated by applicant's amendments.

Lei et al. and Dassa et al. are cited for the reasons set forth in the above rejection.

The difference between the reference and the claims is that Lei does not teach such a construct wherein said construct is a pRS316 plasmid with a GAPDH promoter.

However, Sikorski et al. teach the use of the pRS316 plasmid for expression of proteins in yeast. Sikorski et al. teach that pRS316 comprises the URA3 selectable marker and that such a vector has the advantage that "in addition to the general features afforded the pRS vectors by the pBLUESCRIPT backbone, such as ssDNA production, high plasmid DNA yields and extensive polylinker, unidirectional deletion formation and simplified cloning (blue/white screening for recombinants), these new vectors offer unique yeast-specific features,", i.e. the pRS316 vectors "allow one to perform almost all routine yeast DNA manipulations in the same plasmid" (see page 25, 2nd column, first full paragraph). Sikorski et al also teach that the streamlined design of the pRS vectors makes them well suited to serve as the starting point for construction of other yeast vectors (see entire document, especially paragraph bridging pages 24-25 and page 25, second column, first full paragraph).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the pRS316 vector as taught by Skorski et al with the GAPDH promoter as taught by Lei, because Lei teaches the use of any yeast vector for production of a heterologous protein in yeast and further teaches the use of a GAPDH promoter for expression of the protein and the use of a URA3 selectable marker; Sikorski et al teach that pRS316 is a useful vector for manipulation of DNA (such as cloning) and expression of proteins in yeast and that it comprises a URA3 selectable marker.

One would have been motivated to substitute the pRS316 vector as taught by Sikorski et al in the methods taught by Lei, including the use of the GAPDH promoter, because Sikorski et al teach that the streamlined design of the pRS vectors would make DNA manipulations and cloning easier and Lei teaches that the se of the GAPDH promoter for strong production of a heterologous protein in yeast and the URA3 marker for selection. Based upon the teachings of the cited references, the high ~skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result when utilizing the pRS316 yeast vector as taught by Sikorski et al in the methods and constructs as taught by Lei.

Applicant argues that for the reasons set forth in the previous section, the '572 patent fails to teach or suggest the claim limitation wherein the composition of the protein to be expressed is designed based on the notional requirement of the animal. However, for reasons set forth above, this argument is not found convincing. It is maintained that the claims are not drawn to a method of determining nutritional requirements and designing polypeptides, but rather to a yeast strain comprising any polypeptide which, when added to a food source for an animal, would result in weight gain as compared to the food source alone. It is maintained that any polypeptide would constitute such a polypeptide, since a food source lacking in protein would be adequately supplemented by the polypeptides disclosed in the references to result in weight gain. Therefore the rejection is maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636